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Historical vignette

The history and evolution of transsphenoidal surgery

JAMES K. LIU, M.D., KAUSHIK DAS, M.D., MARTIN H. WEISS, M.D., EDWARD R. LAWS, JR., M.D., AND WILLIAM T. COULDWELL, M.D., PH.D.

Department of Neurosurgery, New York Medical College, Valhalla and New York, New York; Department of Neurosurgery, University of Southern California, Los Angeles, California; and Department of Neurological Surgery, University of Virginia, Charlottesville, Virginia

Initial attempts at transcranial approaches to the pituitary gland in the late 1800s and early 1900s resulted in a mortality rate that was generally considered prohibitive. Schloffer suggested the use of a transsphenoidal route as a safer, alternative approach to the sella turcica. He reported the first successful removal of a pituitary tumor via the transsphenoidal approach in 1906. His procedure underwent a number of modifications by interested surgeons, the culmination of which was A. E. Halstead's description in 1910 of a sublabial gingival incision for the initial stage of exposure. From 1910 to 1925, Cushing, combining a number of suggestions made by previous authors, refined the transsphenoidal approach and used it to operate on 231 pituitary tumors, with a mortality rate of 5.6%. As he developed increasing expertise with transcranial surgery, however, Cushing reduced his mortality rate to 4.5%. With the transcranial approach, he was able to verify suprasellar tumors and achieve better decompression of the optic apparatus, resulting in better recovery of vision and a lower recurrence rate. As a result he and most other neurosurgeons at the time abandoned the transnasal in favor of the transcranial approaches.

Norman Dott, a visiting scholar who studied with Cushing in 1923, returned to Edinburgh, Scotland, and continued to use the transsphenoidal procedure while others pursued transcranial approaches. Dott introduced the procedure to Gerard Guiot, who published excellent results with the transsphenoidal approach and revived the interest of many physicians throughout Europe in the early 1960s. Jules Hardy, who used intraoperative fluoroscopy while learning the transsphenoidal approach from Guiot, then introduced the operating microscope to further refine the procedure; he thereby significantly improved its efficacy and decreased surgical morbidity. With the development of antibiotic drugs and modern microinstrumentation, the transsphenoidal approach became the preferred route for the removal of lesions that were confined to the sella turcica. The evolution of the transsphenoidal approaches and their current applications and modifications are discussed.

KEY WORDS • **neurosurgical history** • **transsphenoidal surgery** • **pituitary tumor**

> If one is to approach the pituitary fossa through the sphenoidal sinuses, it is clear that the only promising, one could almost say justifiable, method is that of Hirsch and Cushing. Especially in the hands of the latter, who adopts the sublabial incision, this operation has been attended by very little risk of meningitis.—Zachary Cope, M.D. (1916)

It has been nearly a century since the first successful attempts to perform surgery on the pituitary gland. The only promising method, as stated by Cope,[14] has withstood the test of time; the transsphenoidal approach to the sella turcica, which is based on the foundations laid by Hirsch and Cushing, continues to be the method of choice for treating most sellar lesions.

Interest in the pituitary gland began as early as 1886 when Pierre Marie[65] described two patients with acromegaly who had enlarged pituitary glands. He postulated that this pituitary hypertrophy was part of the overall acromegalic process. The discovery that hypersecreting pituitary tumors actually caused acromegaly was not made, however, until much later, in 1910. Marie's landmark paper sparked the beginning of neuroendocrine physiology and resulted in the development of surgical approaches to the pituitary gland. Initial approaches to the sella turcica were attempted transcranially. The first recorded attempt at resection of a pituitary tumor was performed by Caton and Paul[10] in 1893; they used a temporal approach suggested by Sir Victor Horsely. The procedure entailed a two-stage lateral subtemporal decompression in a patient with acromegaly. Unfortunately, the tumor was never reached and the patient died 3 months later. Subsequently, between 1904 and 1906, Horsley[48] operated on 10 pituitary tumors by using both subfrontal and lateral middle fossa approaches (Fig. 1), with a mortality rate of 20%.[14]

Evolution of Transcranial Approaches to the Sella Turcica

In 1904, Kiliani[54] performed an extensive bifrontal intradural approach in cadavers in the hope that his procedure

Abbreviations used in this paper: CS = cavernous sinus; CSF = cerebrospinal fluid.

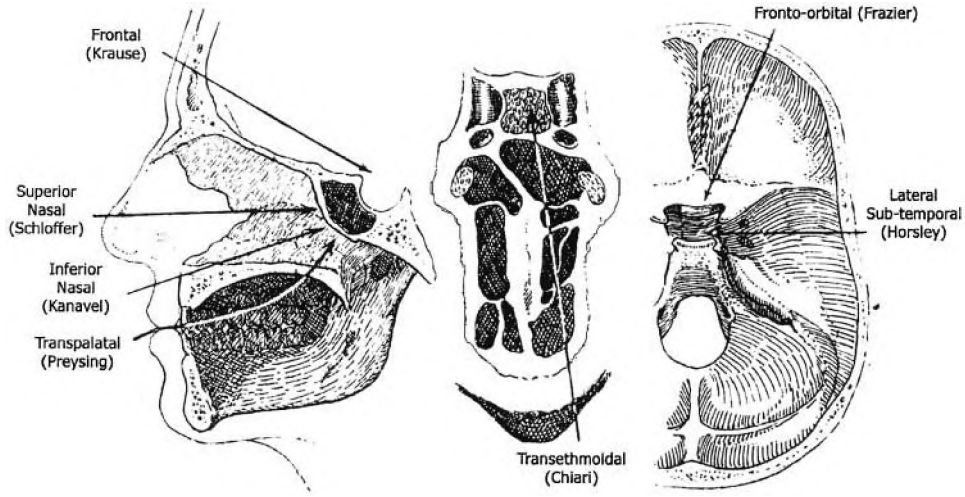


FIG. 1. Drawings showing routes of approach to the pituitary fossa. (Modified with permission from Cope VZ: **Br J Surg 4:**107–144, 1916.)

would offer adequate visualization for total intradural tumor resection. In Berlin in 1905, Fedor Krause[57] used a frontal transcranial approach to reach the sella turcica in a living patient (Fig. 1). This procedure provided the basis from which the majority of subsequent variations on transcranial approaches were developed.[16] McArthur[67] advocated an extradural approach with resection of the supraorbital ridge and the orbital plate to allow dissection to extend posteriorly to the level of the optic chiasm.

These basic approaches were modified and improved by a number of neurosurgical pioneers in the early part of the 20th century, including Dandy,[22] Heuer,[44] Frazier,[27,28] and Cushing.[20,21] These surgeons favored primarily intradural anterior fossa approaches, which are still used by neurosurgeons. Heuer, with the assistance of Walter Dandy, developed a lateral anterior fossa approach by using the landmarks provided by the sphenoid ridge.[22,44] This approach seemed to be the shortest distance between the inner table of the skull and the sella turcica. Frazier's frontoorbital approach, which was a modification of McArthur's procedure, involved resecting the supraorbital ridge and entering intradurally at the midpoint between the midline and the lateral sphenoid wing (Fig. 2).[27,28] This procedure was further used and modified by Charles Elsberg,[25] who made the base of the flap in the midline and removed the supraorbital ridge with the bone flap in one piece. Cushing's transfrontal craniotomy entailed a direct right subfrontal midline approach.[20] As a result of Cushing's commitment to perfecting intracranial approaches and his powerful influence on American neurosurgery, the mainstream neurosurgical teaching during the 1930s and 1940s continued to focus on a transcranial approach to the pituitary gland. By this time, neurosurgery had become a mature discipline with a strong emphasis on intracranial operations.[13]

Transcranial approaches to the sella turcica continued to dominate through the 1950s. Luft and Olivecrona[64] promulgated the use of a transfrontal intradural approach to the pituitary gland while developing extensive experience with hypophyseal ablation for the management of metastatic breast cancer, prostate carcinoma, and diabetic retinopathy. The champion was Bronson Ray,[70] who performed more than 1000 operations for ablative hypophysectomies,[60] and who was able to remove the pituitary gland, from skin incision to the last suture, in less than 1 hour. As related by Zervas,[81] he stated that the best procedure was the simplest, provided that it was safe and effective. Ray also emphasized the need for a properly placed low bone flap to minimize brain retraction.

Evolution of the Transsphenoidal Approach

Early attempts to use transcranial approaches at the turn of the 19th century and shortly thereafter resulted in a mortality rate that was generally considered prohibitive.[13,16] Although Horsley had a mortality rate of 20% in his series of 10 patients, it was significantly better than those of his colleagues, which ranged from 50 to 80%. As a consequence of the high mortality rate for transcranial approaches, surgeons sought safer alternative extracranial routes to the sella turcica.

The first to propose surgical removal of the pituitary gland through a transfacial approach was probably Giordano[30] in 1897. He described a transglabellar–nasal approach based on anatomical studies, in which resection of the anterior wall of the frontal sinus and the nose was used. In this operation, a bilateral paranasal and frontal incision is made, allowing nasal-glabellar degloving. The ethmoid bone is then removed and the olfactory fibers are cut as they pass through the cribriform plate, thus exposing the anterior wall of the sphenoid sinus. As reported in Artico, et al.,[3] Giordano's work laid the foundation for Hermann Schloffer in Innsbruck, Austria, to perform the transsphenoidal operation in a live patient.

Schloffer's Transnasal Approach and Further Modifications

In March 1907, Schloffer reported the first successful removal of a pituitary tumor via a superior nasal transsphenoidal approach, which was based on Giordano's experi-

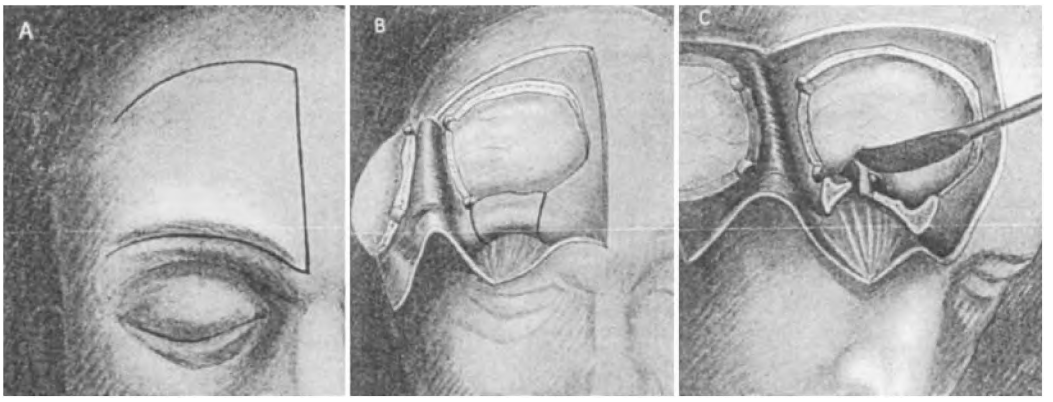


FIG. 2. Drawings showing Frazier's frontoorbital operation in three stages. A: The incision starts at the external angular process and is continued forward along the supraorbital ridge through the eyebrow line until the midline at the root of the nose is reached. It then ascends vertically until the hairline is reached. The incision is then extended laterally to the temporal region. B: The bone flap is made, and a wedge of the outer portion of the supraorbital ridge is removed. C: The periosteum is freed from the roof of the orbit, which is removed with rongeurs to the back of the optic foramen. The orbital contents are displaced down and outward by flat retractors, and the frontal lobe is elevated to visualize the optic nerve as it passes toward the sella turcica. The dura is then incised horizontally 1 cm above the skull base to allow introduction of a retractor to expose sellar contents. (Reprinted with permission from Cope VZ: **Br J Surg 4:**107–144, 1916.)

mental work.[73,74] The description of his transnasal operation details a three-stage procedure in which local anesthesia was produced by cocaine.[14] This procedure was a modification of operations used to treat sphenoid sinus disease. The first stage involved making an incision along the left nasolabial furrow up to the glabella, reflecting the entire nose pedicle to the right, and removing the nasal turbinates and the septum, after application of local anesthesia (Fig. 3A and B). The second stage involved removing the vomer and the rostrum of the sphenoid, followed by opening the sphenoid sinus (Fig. 3C). In the third stage, the mucosa of the sinus was removed and the floor of the sella turcica was opened with a chisel (Fig. 3D). Schloffer's procedure was subsequently performed by von Eiselsberg[77] and Hochenegg in Vienna in 1908. Complications of meningitis and unsatisfactory cosmesis after this disfiguring operation prompted more modifications of the transnasal approach.

In 1909, Theodor Kocher[55] improved the transnasal approach by resecting the septum submucosally, thus allowing better visualization of sellar anatomy (Fig. 4). In the same year, Allen Kanavel[52] in Chicago described an inferior nasal approach in which the external nose was reflected upward and the septum was resected (Fig. 4). Subsequently, Samuel Mixter and Alex Quackenboss[68] used Kanavel's infranasal approach and added the submucous resection of the nasal septum.

In 1910, Oskar Hirsch,[45] a Viennese otorhinolaryngologist, described his classic endonasal transseptal transsphenoidal approach performed with the patient receiving local anesthesia. As detailed by Welbourn,[78] Hirsch reached the nasal septum directly by making an endonasal incision through the nares, thus avoiding a lateral rhinotomy (Fig. 4). A strict midline dissection was maintained, with elevation and separation of mesial mucosal flaps and removal of cartilaginous and bony septum.[36]

The culmination of these modifications was the description by Albert E. Halstead[34] in 1910 of the sublabial gingival incision for the initial stage of sphenoid sinus exposure

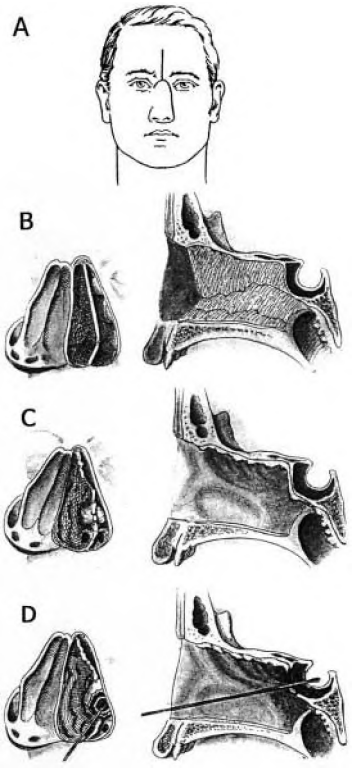


FIG. 3. Drawings showing Schloffer's transnasal transsphenoidal operation. A: An incision is made along the left nasolabial furrow around the left nostril and continued up to the glabella. B: The incision cuts through the skin, nasal bone, philtrum, and the anterior part of the septum. The whole external nose is reflected to the right, exposing the remainder of the septum. C: The rest of the nasal septum has been removed, exposing the rostrum of the sphenoid sinus. D: The anterior wall of the sphenoid sinus is opened, the mucosa lining of the sinus is removed with a sharp spoon, and the floor of the sella turcica is removed with a small chisel or punch forceps. (Reprinted with permission from Cope VZ: **Br J Surg 4:**107–144, 1916.)

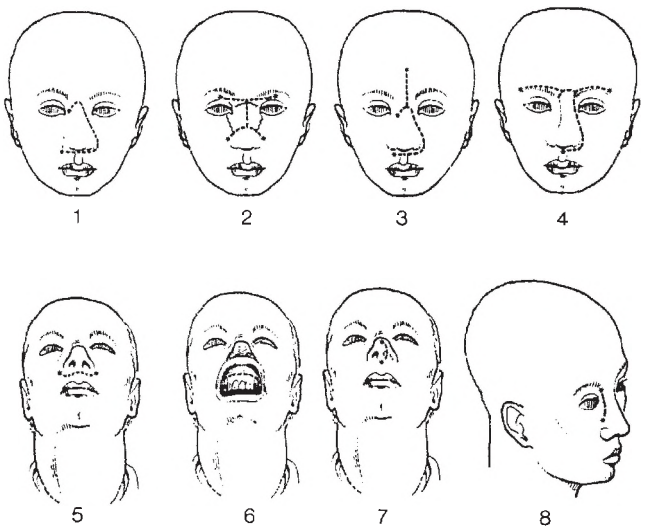


FIG. 4. Drawings showing variations of transsphenoidal approaches. 1: Schloffer's method. 2: Kocher's. 3–4: von Eiselsberg's. 5: Kanavel's. 6: Halstead, Cushing, Dott, Guiot, and Hardy's. 7: Hirsch's. 8: Chiari's. (Modified with permission from Welbourn RB: **Surgery 100:**1185–1189, 1986.)

(Fig. 4). The sublabial incision improved the operative field and left essentially no cosmetic defect.[53,81]

Two other approaches worth mentioning briefly for the sake of completeness include Chiari's transethmoidal approach and Preysing's transpalatal approach. In 1912, Ottokar Chiari[11] described the transethmoidal approach, which consists of a wide ethmoidectomy through an external incision in the superomedial aspect of the orbit (Figs. 1 and 4). Although the transethmoidal approach provided the shortest route to the pituitary gland, the oblique trajectory of this approach did not gain wide acceptance among European neurosurgeons, who preferred a midline approach. Chiari's method was eventually adopted and used for many years by otorhinolaryngologists in Germany, Switzerland, and Scandinavia.[78] One year after Chiari's report was published, Broeckaert[6] related that Preysing in Cologne had described a transpalatal approach, which consists of splitting the soft palate and removing the posterior part of the hard palate, thus allowing access to the sphenoid transorally (Fig. 1). This operation was rarely performed because of complications, which included infection from oral pathogens and postoperative feeding problems.

Cushing's Transsphenoidal Operation

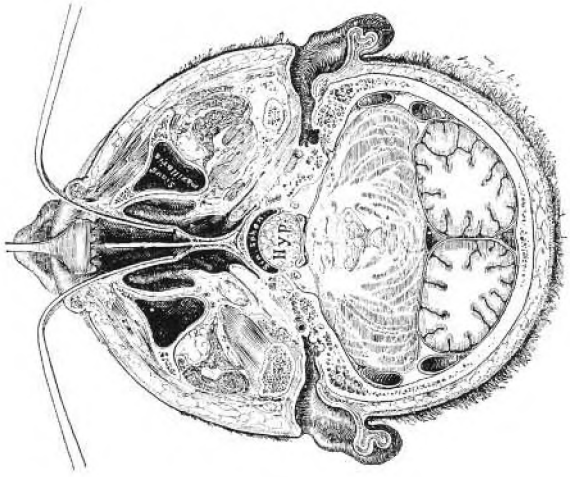
Harvey Cushing (Fig. 5) initially used transcranial approaches for surgical treatment of pituitary tumors, performing eight subtemporal operations (mainly for decompression) and five subfrontal approaches. His initial results were quite discouraging, and as a result, he adopted the alternative transsphenoidal approach.[21] Cushing performed his first transsphenoidal operation in 1909, using Schloffer's procedure in a patient with acromegaly.[19] He later described a modified surgical approach in 1912; in this approach he used A. E. Halstead's sublabial incision and adopted Kocher's submucous septal resection.[20,21] Cushing's modification is essentially the same as the operation

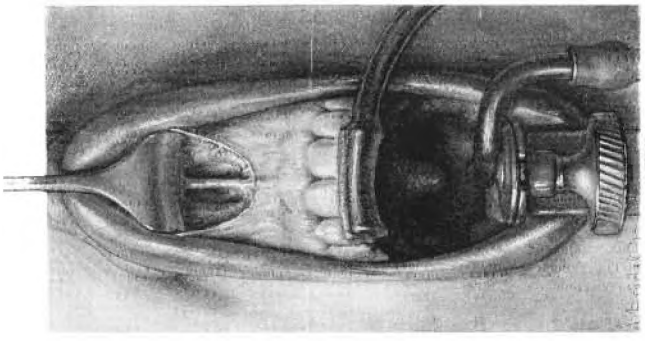
FIG. 5. Photograph of Harvey Cushing. (Reprinted with permission from Laws ER Jr: **Clin Neurosurg 27:**3–18, 1980.)

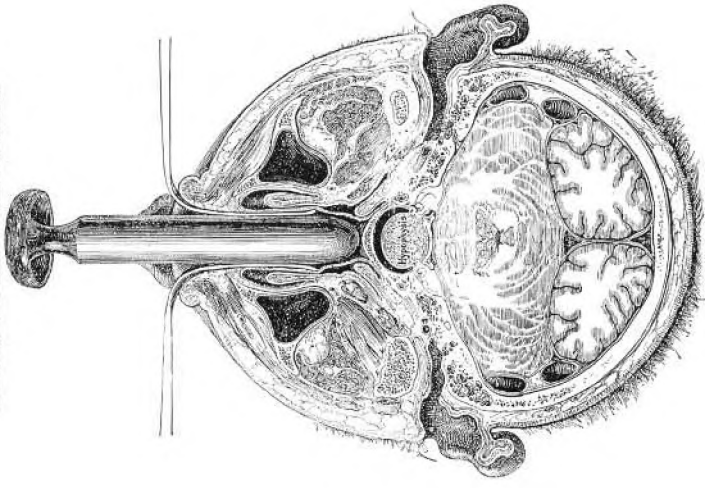
performed by most neurosurgeons today. The operation differed from Hirsch's in that Cushing used intratracheally induced general anesthesia instead of local anesthesia, and that the sublabial incision allowed wider exposure than Hirsch's endonasal approach, which was limited by the diameter of the nostril.[81] A historical coincidence is that both Cushing and Hirsch independently performed the submucous septal resection for the first time on the same day: June 4, 1910.

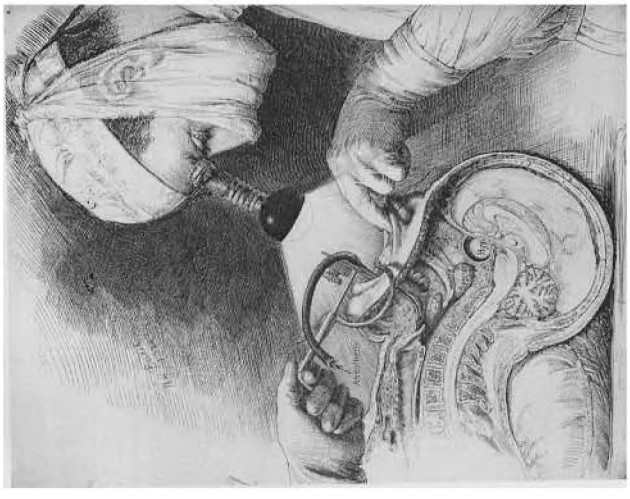
Cushing's transsphenoidal operation is merely a compilation of modifications of Schloffer's operation suggested by several surgeons (Fig. 6 *upper left*). In humility, Cushing[21] stated, "It therefore makes no claim for originality." The first stage involved making a 2-cm transverse incision under the upper lip, and then exposing by blunt dissection the lower margin of the nasal septum (Fig. 6 *upper center*). The mucous membranes are then dissected back from each side of the septum, leaving space for the lateral retractors to be placed (Fig. 6 *upper right*). This allows removal of most of the septum, including most of the vomer and the perpendicular plate of the ethmoid (Fig. 6 *lower left*). Dilating plugs are introduced between the retractor blades to flatten the lower turbinates (Fig. 6 *lower center*). Subsequently, a self-retaining bivalve speculum (a modified pediatric vaginal speculum) is inserted in place of the retractors (Fig. 6

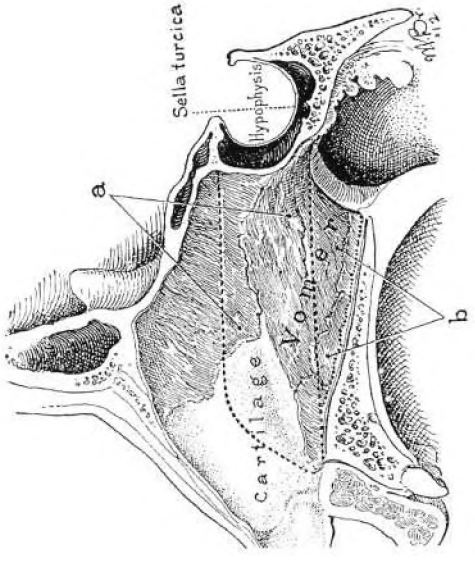
FIG. 6. *Upper Left:* Drawing made in 1912 by renowned medical illustrator Max Brödel, showing Cushing's adaptation of the transsphenoidal approach to the hypophysis. *Upper Center:* A sublabial incision is made and the mucous membrane is elevated, exposing the lower edge of the cartilaginous septum. *Upper Right:* Axial section showing the placement of lateral retractors between the mucous membranes dissected back from each side of the denuded septum. *Lower Left:* Sagittal diagram showing approximately the amount of septum removed with a Ballenger knife. *Lower Center:* Axial diagram showing one of a series of dilating plugs introduced between the lateral retractors to flatten the lower turbinates. *Lower Right:* Sagittal diagram showing the substitution of the two lateral retractors for a self-retaining bivalve speculum through which other surgical instruments are introduced. Note the intratracheal anesthesia apparatus used by Cushing. (Reprinted with permission from Cushing H: **JAMA 63:**1515–1525, 1914. Copyrighted 1914, American Medical Association.) →






Hypophysis




Sella turcica
Hypophysis
a
b
Cartilage
Vomer

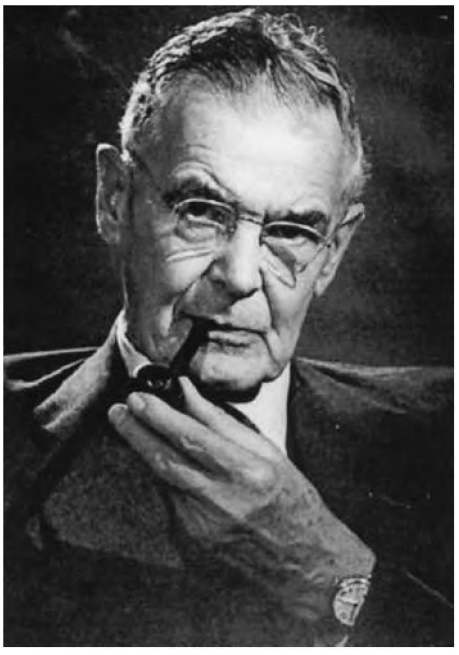


FIG. 7. Photograph of Norman Dott of Edinburgh. This pupil of Cushing preserved the transsphenoidal approach and achieved excellent results. (Reprinted with permission from Laws ER Jr: **Clin Neurosurg 27:**3–18, 1980.)

lower right). Under direct vision aided by a headlight, the sphenoid sinus is then entered with special rongeurs. The lining of the mucous membrane of the sinus is then removed and the floor of the sella turcica is exposed and opened with a chisel. Cushing emphasized that "every step must be absolutely under the operator's direct vision."[21]

FIG. 8. Photograph of Gerard Guiot of Paris. He learned the transsphenoidal approach from Dott and is largely responsible for its revival. Guiot was also an accomplished organist and student of Catholic theology—his two major hobbies. (Reprinted from **Surg Neurol 11**, Hardy J: Neurosurgeon of the year: Gerard Guiot, 1979, with permission from Elsevier Science.)

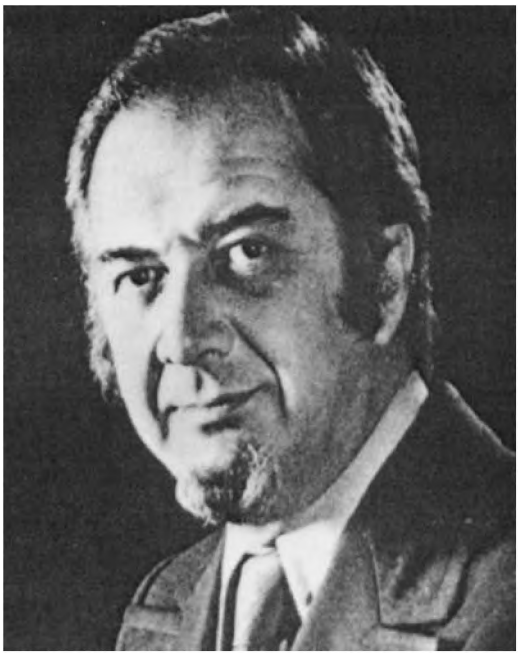


FIG. 9. Photograph of Jules Hardy of Montreal. (Reprinted with permission from Laws ER Jr: **Clin Neurosurg 27:**3–18, 1980.)

Abandonment of the Transsphenoidal Approach

As reported by Henderson,[43] Cushing used the transsphenoidal approach between 1910 and 1925 to operate on 231 pituitary tumors, with a mortality rate of only 5.6%. This represented the best efforts at surgical exposure and access to the pituitary gland at the time. Incidences of morbidity and mortality from the transsphenoidal approach were primarily the result of infection, which was frequently associated with postoperative CSF rhinorrhea, hemorrhage, and postoperative edema.

Meanwhile, Cushing also had an intense interest in intracranial surgery, which contributed to his pursuit and development of transcranial approaches to the pituitary gland. Over the next few decades, as he developed expertise and confidence in these approaches, he reduced his mortality rate with the transcranial approach to 4.6%, essentially eliminating any significant difference in surgical mortality between that and the transsphenoidal approach.[16] Henderson[43] commented, "The danger of meningitis after the transsphenoidal operation is counterbalanced by the slight risk of clot formation after the transfrontal operation." Rosegay[71] reported that Cushing used both approaches impartially, choosing the one that best served the patient.

By the late 1920s, Cushing treated many patients with suprasellar tumors, especially meningiomas and craniopharyngiomas, which were indistinguishable preoperatively from large pituitary tumors that were surgically inaccessible from below.[78] The transfrontal approach, as described by Krause and Frazier, enabled Cushing to verify suprasellar tumors diagnostically and achieve a more extensive resection and a more complete decompression of the optic nerve and chiasm. As a result, his patients experienced better recovery of vision and a lower recurrence rate for tumors resected transfrontally. A craniotomy also avoided the dreaded complication of systemic infection, the most

frequent cause of death in the transsphenoidal approach. By 1929 to 1931, the last years of his active neurosurgical practice, Cushing had virtually abandoned the transsphenoidal operation, performing pituitary surgery exclusively via the transfrontal route.[16,43,71] Because of Cushing's outstanding results with the alternative route and his dominance in American neurosurgery, the use of transsphenoidal operations in the pituitary gland declined profoundly for the next 35 years. During this time, however, Norman Dott, who learned the transsphenoidal approach from Cushing during a traveling fellowship at the Peter Bent Brigham Hospital in 1923, returned to the Royal Infirmary of Edinburgh where he continued to practice this procedure.[23] This crucial event in neurosurgical history paved the way for the preservation, and later the reemergence, of transsphenoidal surgery.

A few other surgeons, such as Hirsch[46,47] and Hamlin,[35] continued to use the transsphenoidal approach, with reports of excellent long-term results. As related by Hamlin,[36] Hirsch immigrated to Boston in 1938 after being expelled from Austria by the Nazis. Because Hirsch was not allowed to operate independently at Massachusetts General Hospital, he collaborated with Hannibal Hamlin, a neurosurgeon in the Boston community. With Hamlin's assistance, Hirsch attempted to maintain the popularity of the transsphenoidal approach, but remained an "obscure voice in the wilderness."[81] Despite Hirsch's efforts, transfrontal approaches dominated the surgical management of pituitary tumors through the 1950s and early 1960s.

Resurrection of the Transsphenoidal Approach

The existence of the transsphenoidal approach appeared tenuous after Cushing's complete conversion to transcranial procedures. One of Cushing's pupils, Norman Dott (Fig. 7) of Edinburgh, valued the importance of the transsphenoidal operation, however, and performed it when indicated. Dott recognized that the transsphenoidal procedure had fallen into undeserved neglect because of the widespread popularity of transcranial operations.[4] According to Horwitz,[49] by 1956, Dott had performed 80 consecutive transsphenoidal operations with no deaths and had also developed a lighted speculum retractor that improved illumination of the surgical site.

Dott subsequently introduced his method to Gerard Guiot, an innovative French neurosurgeon (Fig. 8). Guiot witnessed Dott's meticulous technique while at the Royal Infirmary in 1956. Impressed by the simplicity and neatness of the procedure and Dott's outstanding surgical outcomes, Guiot was converted into a firm believer in the transsphenoidal approach. Back in Paris, Guiot sought to revive the transsphenoidal approach in a country where it was practically forsaken. In 1959 he wrote, "Its advantages should be reconsidered and its indications retained. . . . Shouldn't one stop referring to this approach as 'historic' and 'passé'? Isn't it right to admit its advantages and retain its indications? Without doubt."[33,71]

In 1957, Guiot started to perform the transsphenoidal approach and subsequently accrued a series of more than 1000 cases of pituitary adenomas treated surgically. As reported by Hardy and Wigser,[42] he further enhanced surgical accuracy by using intraoperative radiofluoroscopic control to define clearly the anatomy of the nasal passages while maneuvering surgical instruments. Guiot mastered the technique of combining transsphenoidal decompression and postoperative radiation to achieve the best results. Led by his pioneering spirit, Guiot applied the transsphenoidal approach in treating craniopharyngiomas, clival chordomas, and parasellar lesions. As a result of his numerous contributions, he became the pivotal figure in the spread of the transsphenoidal approach and its resurrection over the following two decades.[31,32,38,81] Its revival is best summarized by Jules Hardy: "the transsphenoidal operation is again being employed in Europe by two neurosurgeons of great renown, Norman Dott of Edinburgh who preserved it, and Guiot of Paris who has taken it up again and perfected it."[37]

Jules Hardy: A New Era of Transsphenoidal Microsurgery

Jules Hardy of Montreal (Fig. 9) worked as a fellow under Guiot to learn his method. Hardy continued Guiot's use of televised radiofluoroscopic control, which allowed him to perform more extensive resections of large midline suprasellar tumors and avoid opening the arachnoid membranes, which results in CSF fistulas. By 1965, he had adopted routine use of preoperative angiography and intraoperative air encephalography. In 1967, Hardy introduced the use of the operating microscope for this procedure,[39] and developed and designed his own microsurgical instrumentation, which transformed transsphenoidal surgery (Fig. 10 *upper left*). The use of the microscope permitted safer and more effective resections of pituitary tumors and other sellar and parasellar lesions. No deaths or serious morbidities occurred in the first 50 patients who underwent microsurgery.[78]

In 1968, Hardy[41] introduced the concept of the microadenoma, which caused endocrinological abnormalities without deformation of the bony sella turcica. He advocated early detection of microadenomas before they invaded local structures, and he performed selective removal of these lesions while preserving pituitary function. Hardy's illustrative landmark paper in 1971[40] on the technical aspects of his transsphenoidal operation described at great length the use of the operating microscope for improved illumination as well as intraoperative fluoroscopic guidance to control the position of the instruments introduced into the suprasellar area for complete removal of pituitary adenomas (Fig. 10). He described the use of this procedure in more than 300 patients to perform total hypophysectomy, selective removal of microadenomas, removal of craniopharyngiomas, and removal of sellar or clival chordomas and meningiomas. The rate of morbidity and mortality was less than that of transcranial approaches, and the risk of CSF rhinorrhea was reduced considerably when the arachnoid was left intact.

The procedure described by Hardy has undergone many refinements and has been the fundamental and principal surgical procedure used by most neurosurgeons for the removal of pituitary tumors and other sellar lesions for the last 30 years.[15,17,18,29,60,61,63,69] Most experienced neurosurgeons have reported mortality rates between 0% and 1%, rendering the procedure reasonably safe and effective.[5,12,60,62,79] It is performed widely in the Americas and Europe, and several neurosurgeons have each used this approach to per-

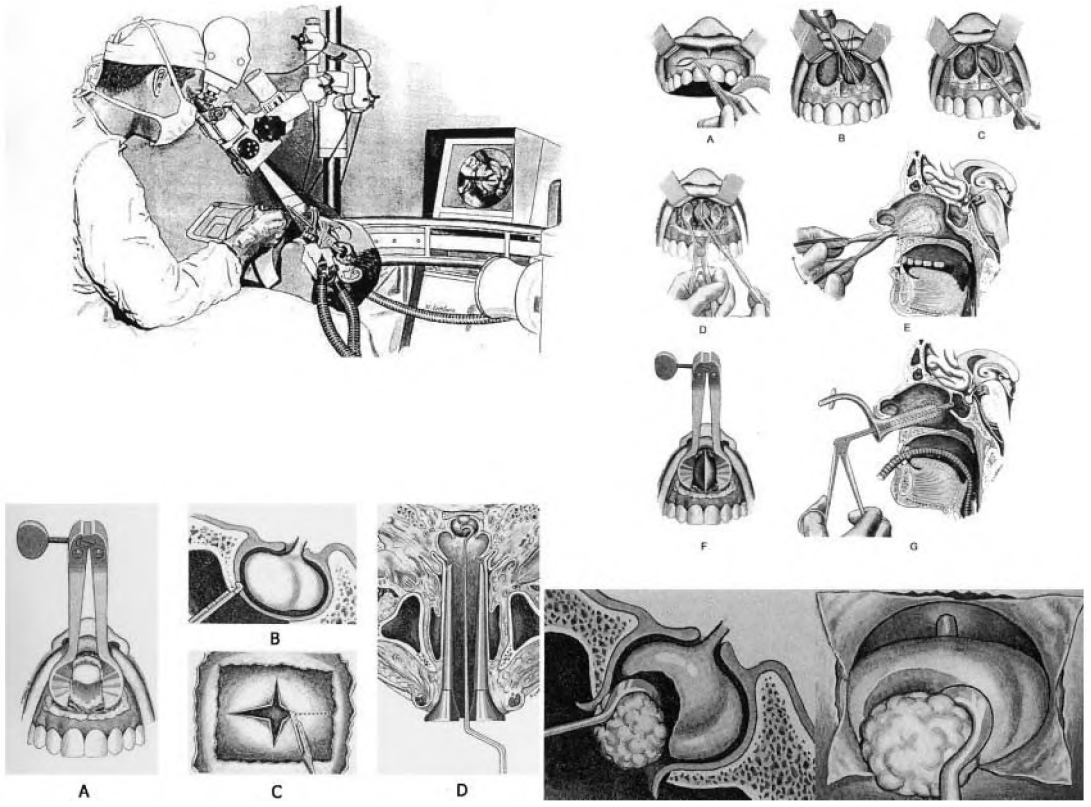


FIG. 10. *Upper Left:* Illustration depicting Hardy's use of the operating microscope and televised radiofluoroscopic control. *Upper Right:* Illustrations showing Hardy's sublabial transseptal transsphenoidal approach. A: Sublabial incision. B: Elevation of nasal mucosa from the floor. C: Submucosal dissection from the septum. D: Resection of the cartilaginous septum with a swiveled knife. E: Sagittal view of the submucosal dissection. F: Introduction of the self-retaining speculum that reveals the vomer, which resembles the keel of a ship. G: Sagittal view of the speculum in position. *Lower Left:* Operative drawing showing the sella turcica portion of the procedure. A: Resection of the vomer and the floor of the sphenoid sinus, exposing the sella turcica. B: Opening of the sellar floor with a rongeur. C: Cruciate incision made in the dura of the sella turcica. D: Horizontal view of the strict midline approach to the sella turcica. *Lower Right:* Drawing showing selective removal of a pituitary microadenoma while preserving pituitary function. (Reprinted with permission from Hardy J: **J Neurosurg 34:**582–594, 1971.)

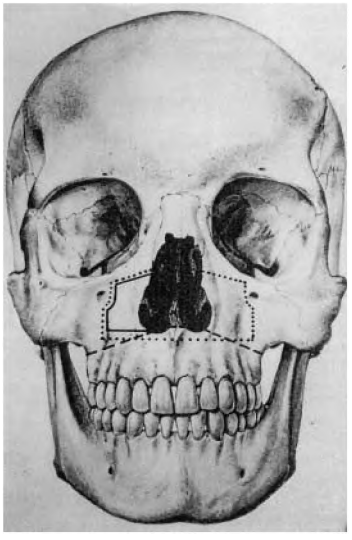


FIG. 11. Drawing showing osteotomies used in the transmaxillosphenoidal approach: unilateral maxillary *(solid line)*, bilateral maxillary *(dotted line)*, and Le Fort osteotomies *(dashed line)*. (Reprinted with permission from Fraioli B, et al: **J Neurosurg 82:** 63–69, 1995.)

form more than 1000 procedures, most notably Edward Laws with 3580 cases and Charles Wilson with 3182 cases to date (CB Wilson, personal communication, 2001).

One may question why the transsphenoidal approach remained obscure for nearly 35 years before it regained widespread acceptance. First, effective antibiotic medications were not available until the 1950s.[81] Their introduction reduced the rate of surgical mortality caused by systemic infection, which was once thought to be prohibitive. Second, the introduction of corticosteroid replacement therapy allowed safer surgery on the pituitary gland, especially in patients who underwent total hypophysectomy.[78] Finally, one may postulate that the lack of proper illumination and the low familiarity with this method among neurosurgeons also contributed to the delayed resurrection of the transsphenoidal approach.

Evolution of Extended Transsphenoidal Modifications

In the last decade, the classic transsphenoidal approach described by Hardy[40] has undergone further transformation. Regions of the skull base that were once thought to be ac-

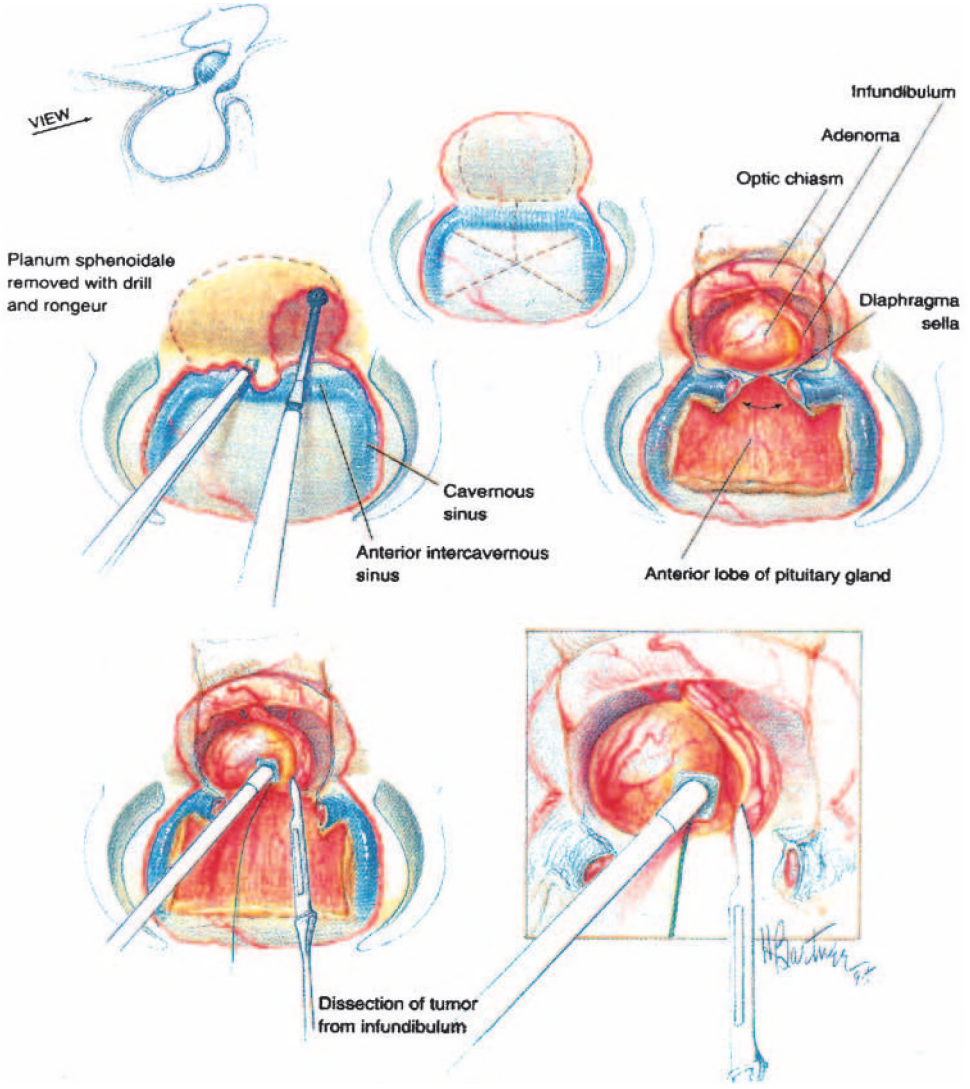


FIG. 12. Drawings showing the modified transsphenoidal approach used to access the suprasellar cistern. A wide bone exposure of the anterior surface of the sella turcica and subsequent bone removal exposes the medial portion of the CS bilaterally. The posterior portion of the planum sphenoidale is removed using a high-speed drill and Kerrison rongeur to access the suprasellar cistern. Tumors in this region can be safely removed via a transsphenoidal approach. (Reprinted with permission from Mason RB, et al: **J Neurosurg 87:**343–351, 1997.)

cessible only from above are now being approached transfacially. With better knowledge of microsurgical anatomy and modern microinstrumentation, neurosurgeons have modified the transsphenoidal approach to gain better access to regions such as the CS and the suprasellar cisterns.

Fraioli and coworkers[26] used a transmaxillosphenoidal approach to treat 11 patients with sellar tumors that had invaded the medial wall of the CS. In addition to the standard transsphenoidal exposure, this approach involves a unilateral, bilateral, or Le Fort maxillary osteotomy and removal of the medial wall of the maxillary sinus (Fig. 11). This exposure allows direct visualization of the intracavernous carotid artery during tumor resection; however, extension of tumor lateral to the carotid artery poses limitations for this approach.

Sabit and colleagues[72] have recently described a safe, minimally invasive combined transmaxillary transsphenoidal approach to the CS that is both extradural and extranasal. Through a sublabial incision and maxillotomy, the course of the infraorbital nerve (the terminal branch of V2) is identified and followed back to the foramen rotundum, leading to the cranial base and the floor of the middle fossa. This approach provides adequate lateral-to-medial reach in the parasellar and infrasellar regions, with visualization of the entire ipsilateral CS and the medial aspect of the contralateral CS.

Suprasellar tumors without sellar enlargement, which are traditionally approached transcranially, have been successfully resected by Kouri, et al.,[56] and Mason, et al.,[66] by using a modified transsphenoidal approach. This involves a wide bone exposure of the anterior surface of the sella turcica, followed by removal of the posterior portion of the planum sphenoidale with a high-speed drill and Kerrison rongeur (Fig. 12). The dura overlying the planum sphenoidale is

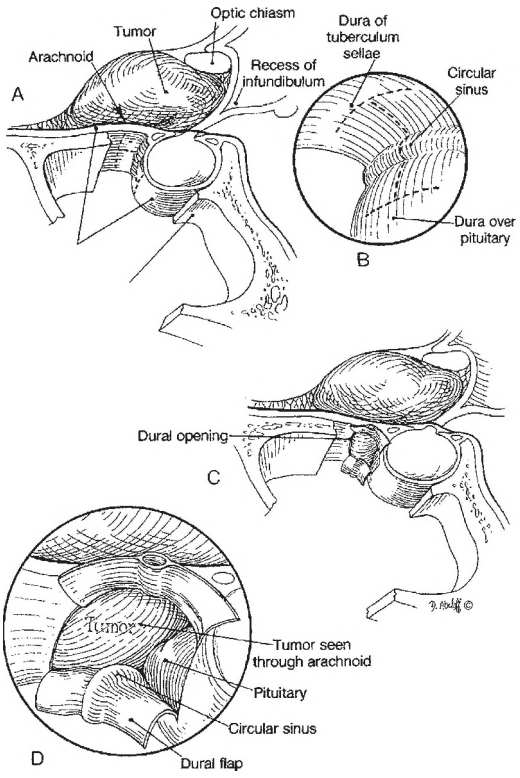


FIG. 13. Drawings showing the extended transsphenoidal approach with exposure of the anterior skull base. A purely suprasellar tumor may be approached by extending the bone resection anteriorly over the tuberculum sellae, thus exposing the dura mater lying anterior to the circular sinus. An incision is made in the dura mater anteriorly and inferiorly to the circular sinus. The sinus is then coagulated and transected to gain a direct view of the suprasellar cistern without disturbing the pituitary gland. (Reprinted with permission from Couldwell WT and Weiss MH, in Apuzzo MLJ (ed): **Surgery of the Third Ventricle, ed 2.** Baltimore: Williams & Wilkins, 1998.)

opened, providing access to the suprasellar cistern as well as the medial aspect of each CS. This novel approach has allowed resection of craniopharyngiomas, central nervous system hemangioblastomas, and ectopic adrenocorticotropic hormone–producing adenomas arising from the pituitary stalk.

Extension of transsphenoidal approaches to gain additional exposure of the skull base for lesions of the parasellar and clival region has recently been reviewed and refined by Couldwell and Weiss.[18] Combining an alteration of the position of the self-retaining retractors and the use of an asymmetric retractor (to enable cross-court lateral visualizations), various portions of the skull base may be exposed and bone resection can be extended in the superior/inferior and lateral directions, respectively. With these modifications, the extended transsphenoidal approach provides exposure for removal of tumors growing beyond the traditional boundaries of the sella turcica and suprasellar cistern; the approach may be extended anteriorly to resect suprasellar lesions, inferiorly to expose clival lesions, and laterally to access CS lesions (Figs. 13–15).

Transsphenoidal Surgery in the New Millennium

Technological advances in the areas of endoscope-assisted microneurosurgery,[1,8,50,51] frameless stereotaxy and three-dimensional computer-assisted neuronavigation,[24] color Doppler ultrasonography,[2] and real-time intraoperative magnetic resonance imaging[76] have been applied to the classic transsphenoidal operation in an attempt to decrease morbidity and mortality rates further.

Bushe and Halves[7] reported the first use of the endoscope in pituitary surgery in 1978. Its application to the sella turcica did not grow in popularity, however, until the mid-1990s, when endoscopic sinus surgery had virtually replaced conventional open techniques in use by otolaryngologists for the treatment of inflammatory sinonasal disorders. The excellent visualization and surgical results pro-

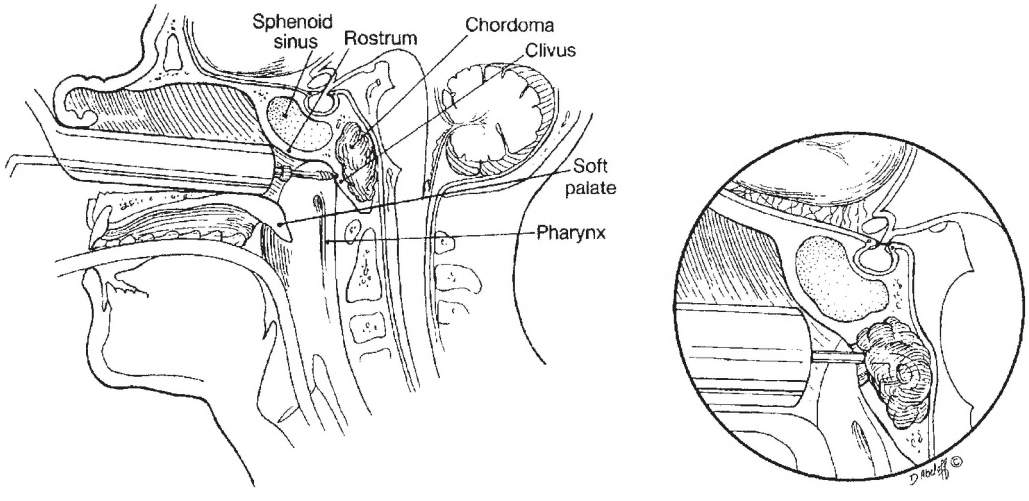


FIG. 14. Drawings showing the extended transsphenoidal approach with inferior exposure of the clivus. Exposure of the clivus is facilitated by slight flexion of the patient's head and repositioning of the nasal self-retaining retractor to point inferiorly. The upper clivus lies directly posterior to the sphenoid sinus, but additional exposure of the middle and lower clivus requires more inferior exposure. (Reprinted with permission from Couldwell WT and Weiss MH, in Apuzzo MLJ (ed): **Surgery of the Third Ventricle, ed 2.** Baltimore: Williams & Wilkins, 1998.)

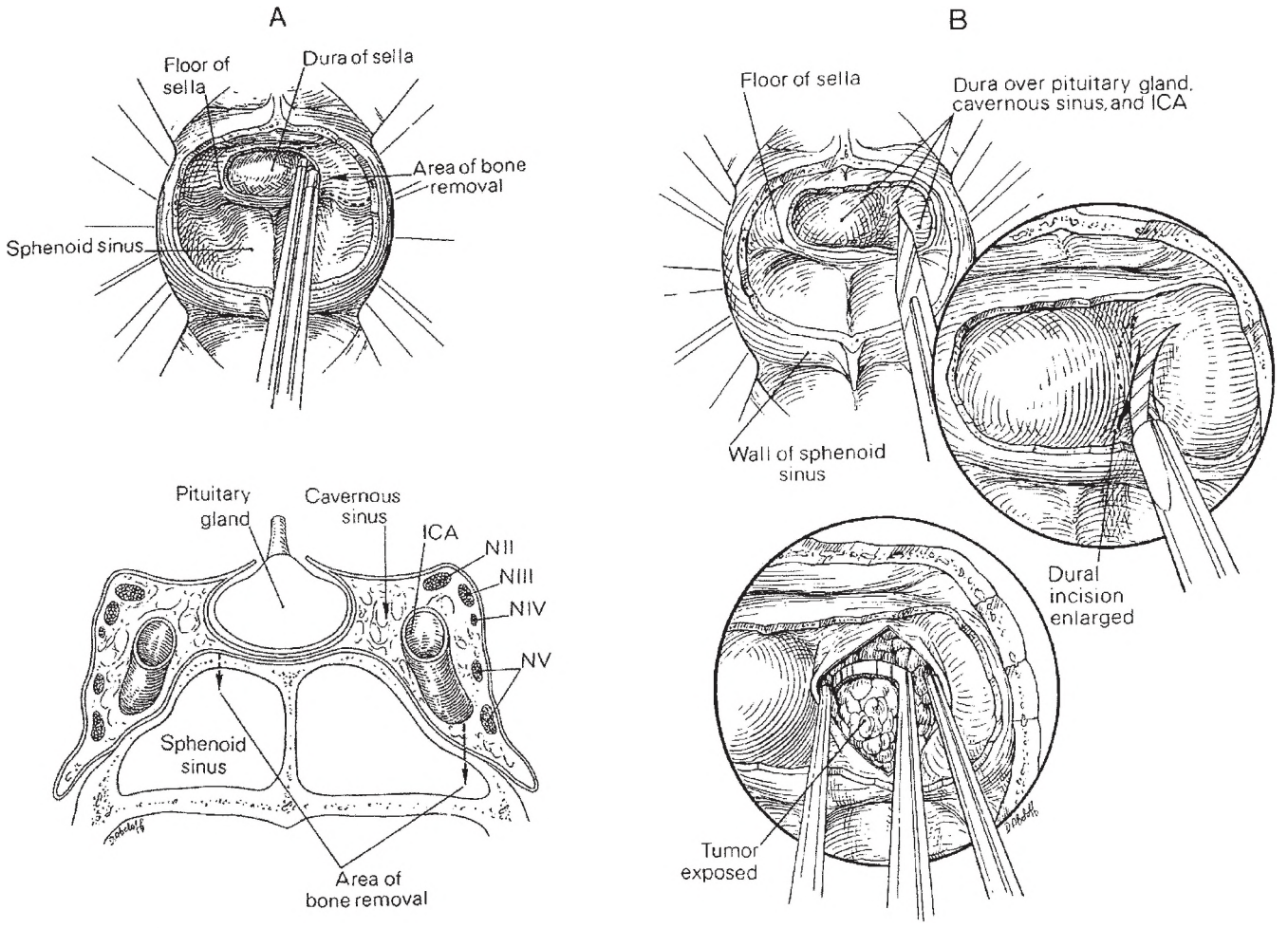


FIG. 15. Drawings showing the extended transsphenoidal approach with inferolateral exposure of the CS. A: After exposure of the dura mater overlying the sella turcica, the bone overlying the CS, including that overlying the carotid grooves, is carefully removed. This removal defines the lateral extent of the exposure limited by the CS cranial nerves. B: The dura mater medial to the internal carotid artery is first incised with a No. 11 blade and opened with curved alligator microscissors. Removal of the intracavernous portion of the tumor is accomplished with a microcurette. (Reprinted with permission from Couldwell WT and Weiss MH, in Apuzzo MLJ (ed): **Surgery of the Third Ventricle, ed 2.** Baltimore: Williams & Wilkins, 1998.)

vided by the endoscope in sinus surgery have prompted neurosurgeons to explore its potential application to transsphenoidal surgery.[1,9,51]

Several variations in the procedure regarding the use of the endoscope in transsphenoidal surgery have been reported in the literature. Yaniv and Rappaport[80] described a combined approach in which the endoscope was used for the initial approach to the sphenoid sinus, followed by conversion to the standard transsphenoidal microsurgical approach for the tumor resection. This allows decreased nasal morbidity for the approach while taking advantage of the stereoscopic vision offered by the operative microscope. Angled endoscopes can then be used to inspect for residual tumor that may normally be outside the surgeon's view.

Jho and Carrau[50] have reported the largest series of patients (50) who have undergone endoscopic endonasal transsphenoidal surgery, with encouraging results. They described an endoscopic approach in which only one nostril is entered, with the endoscope held in the surgeon's nondominant hand and surgical instruments held in the dominant hand (Fig. 16). Once the anterior sphenoidotomy is made, the endoscope is mounted, freeing up both hands to maneuver instruments. The authors claim that the endoscopic approach facilitates faster postoperative recovery and reduction of hospitalization times, but this has been contested by experienced pituitary surgeons.[58,59] One of its main advantages is excellent panoramic visualization of the sellar and suprasellar anatomy, with increased illumination and magnification.[51] Anatomical studies performed on cadaver heads at our institution demonstrated that the endoscope provided a superior volume of exposure compared with the operating microscope.[75]

The main criticisms of endoscopic transsphenoidal surgery include the lack of stereoscopic vision and the lack of adequate instrumentation. Working through the limited space of one nostril can also pose potential conflicts, especially between the surgeon's hands and the endoscope.[1] The endoscopic procedure offers many advantages of a mini-

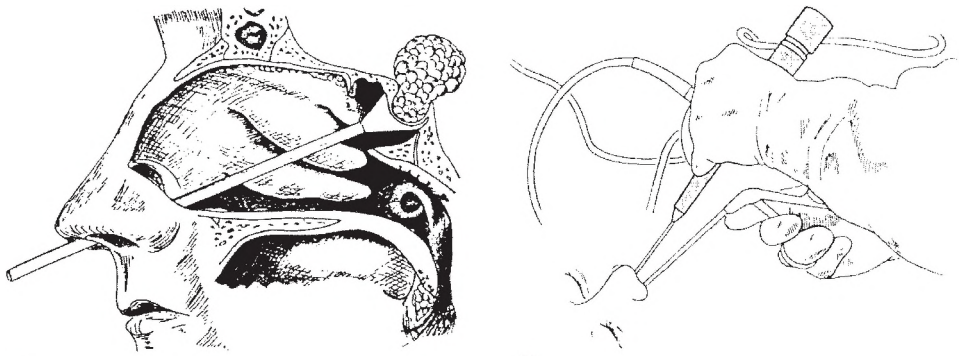


FIG. 16. Drawings showing an endonasal endoscopic approach to the sella turcica. A: Note the absence of septal or alar incisions. No speculum or retractor is used. B: The endoscope is held in the surgeon's nondominant hand and instruments are held in the dominant hand until the anterior sphenoidotomy is made. (Reprinted from **Surg Neurol 47**, Jho HD, et al: Endoscopic pituitary surgery: an early experience, 1997, with permission from Elsevier Science.)

mally invasive method, with satisfying preliminary results; however, there is a learning curve for its use. Whether these procedures will lead to more effective management of sellar lesions awaits longer follow-up studies and additional experience.

Conclusions

In the early 1900s the transnasal approach to the sella turcica was first attempted as an alternative to transcranial approaches because of their high morbidity and mortality rates. Through the contributions of Schloffer, Kanavel, Hirsch, and Cushing, significant improvements were made as the procedure evolved from 1910 to 1925. Although Cushing himself published the results of the transnasal approach in 231 patients and his mortality rate was only 5.6%, he abandoned it in favor of transcranial approaches because he believed that with these the optic apparatus could be immediately decompressed. Because of his dominance in the field, transnasal approaches were largely abandoned. Fortunately, Dott was committed to approaching the sella turcica transsphenoidally and continued to achieve excellent results. Revival of the transsphenoidal approach began in the late 1960s, led by the efforts of Guiot and Hardy. Refinements were made, including the addition of intraoperative fluoroscopy and the operative microscope, which advanced transnasal surgery into the contemporary era. Currently it is the preferred approach for lesions confined to the sella turcica and parasellar regions, and in some cases lesions of the clivus as well. Furthermore, newly described modifications of this classic approach have been used to gain access to the CS and suprasellar regions. Recently, efforts have been made to use frameless stereotaxy, real-time intraoperative imaging, and the endoscope in an attempt to reduce the morbidity rates further while maintaining and improving the effectiveness of the approach.

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Address reprint requests to: William T. Couldwell, M.D., Ph.D., Department of Neurosurgery, New York Medical College, Munger Pavilion, Valhalla, New York 10595, email: william_couldwell@nymc.edu.